

Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition
1	BRS	L1	769 (glucagon-like adj peptide) or glp-1 or glp-2	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 15:36		0
2	BRS	L2	2275 lipophilic adj (substituent or group)	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 15:38		0
3	BRS	L3	18531 fatty adj acid	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 15:39		0
4	BRS	L4	82 1 same (2 or 3)	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 15:40		0
5	BRS	L5	412 spacer same ((succinic adj acid) or glu or asp)	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 16:39		0
6	BRS	L6	4 4 same 5	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 16:00		0
7	BRS	L7	2 6458924.pn.	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 16:39		0
8	BRS	L8	3630 spacer same (lys or glu or asp or gly-lys)	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 17:01		0
9	BRS	L9	6 4 same 8	USPAT; US-PGPUB; EPO; DERWENT	2003/02/2 4 17:01		0
10	BRS	L10	18 jonassen adj ib.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/2 4 17:10		0
11	BRS	L11	34 havelund adj svend.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/2 4 17:10		0

Type	L #	Hits	Search Text	DBs	Time Stamp	Comments	Error Definition
12	BRS	L14 5	hansen adj per adj hertz.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/2 4 17:11		0
13	BRS	L15 5	halstrom adj john.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/2 4 17:12		0
14	BRS	L16 4	(10 or 11 or 14 or 15) and 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/02/2 4 17:12		0

FILE 'HOME' ENTERED AT 17:44:50 ON 24 FEB 2003

=> file medline caplus biosis embase scisearch agricola  
 COST IN U.S. DOLLARS SINCE FILE TOTAL  
 ENTRY SESSION  
 FULL ESTIMATED COST 0.21 0.21

FILE 'MEDLINE' ENTERED AT 17:45:13 ON 24 FEB 2003

FILE 'CAPLUS' ENTERED AT 17:45:13 ON 24 FEB 2003  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
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FILE 'BIOSIS' ENTERED AT 17:45:13 ON 24 FEB 2003  
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FILE 'EMBASE' ENTERED AT 17:45:13 ON 24 FEB 2003  
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FILE 'SCISEARCH' ENTERED AT 17:45:13 ON 24 FEB 2003  
COPYRIGHT (C) 2003 Institute for Scientific Information (ISI) (R)

FILE 'AGRICOLA' ENTERED AT 17:45:13 ON 24 FEB 2003

=> s (glucagon-like peptide) or glp-1 or glp-2  
4 FILES SEARCHED...

L1 10431 (GLUCAGON-LIKE PEPTIDE) OR GLP-1 OR GLP-2

=> **s** lipophilic (w) (substituent or group)

**L2 1546 LIPOPHILIC (W) (SUBSTITUENT OR GROUP)**

=> s fatty acid

### L3 704208 FATTY ACID

=> s 11 (p) 12

L4 8 L1 (P) L2

=> s (succinic acid) or glu or asp or lys or gly-lys

5 FILES SEARCHED...

L5 237276 (SUCCINIC ACID) OR GLU OR ASP OR LYS OR GLY-LYS

=> s 15 (p) spacer

L6 881 L5 (P) SPACER

=> s l1 (p) l3 (p) substituent

L7 5 L1 (P) L3 (P) SUBSTITUENT

=> s l4 or l7

L8 13 L4 OR L7

=> s l8 (p) l6

L9 0 L8 (P) L6

=> s l8 (p) spacer

L10 0 L8 (P) SPACER

=> duplicate remove l8

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE,  
SCISEARCH'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L8

L11 8 DUPLICATE REMOVE L8 (5 DUPLICATES REMOVED)

=> d l11 1-8 ibib abs

L11 ANSWER 1 OF 8 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS  
INC.

ACCESSION NUMBER: 2002:609774 BIOSIS

DOCUMENT NUMBER: PREV200200609774

TITLE: Derivatives of GLP-1 analogs.

AUTHOR(S): Knudsen, Liselotte Bjerre (1); Huusfeldt, Per Olaf;  
Nielsen, Per Franklin

CORPORATE SOURCE: (1) Valby Denmark

ASSIGNEE: Novo Nordisk A/S, Bagsvaerd, Denmark

PATENT INFORMATION: US 6458924 October 01, 2002

SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Oct. 1, 2002) Vol. 1263, No. 1, pp. No  
Pagination. <http://www.uspto.gov/web/menu/patdata.html>.  
e-file.  
ISSN: 0098-1133.

DOCUMENT TYPE: Patent

LANGUAGE: English

AB The present invention relates to a pharmaceutical composition comprising a  
\*\*\*GLP\*\*\* - \*\*\*1\*\*\* derivative having a \*\*\*lipophilic\*\*\*

\*\*\*substituent\*\*\* ; and a surfactant.

L11 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2003 ACS DUPLICATE 1  
ACCESSION NUMBER: 2001:721487 CAPLUS

DOCUMENT NUMBER: 135:273221

TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles

INVENTOR(S): Knudsen, Liselotte; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy Zimmerdahl; Madsen, Kjeld

PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.

SOURCE: U.S., 136 pp., Cont.-in-part of U.S. Ser. No. 38,432, abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6268343	B1	20010731	US 1999-258750	19990226
WO 9808871	A1	19980305	WO 1997-DK340	19970822
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2001011095	A2	20010116	JP 2000-152778	19970822
ZA 9901571	A	19990902	ZA 1999-1571	19990226
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
US 2002025933	A1	20020228	US 2001-908534	20010718
PRIORITY APPLN. INFO.: DK 1996-931 A 19960830				
DK 1996-1259 A 19961108				
DK 1996-1470 A 19961220				
US 1997-36255P P 19970124				
US 1997-36226P P 19970125				
WO 1997-DK340 A2 19970822				
US 1997-918810 B2 19970826				
DK 1998-263 A 19980227				
DK 1998-264 A 19980227				
DK 1998-268 A 19980227				
DK 1998-272 A 19980227				
DK 1998-274 A 19980227				
US 1998-38432 B2 19980311				

DK 1998-508 A 19980408  
DK 1998-509 A 19980408  
US 1998-82478P P 19980421  
US 1998-82480P P 19980421  
US 1998-84357P P 19980421  
US 1998-82802P P 19980423  
US 1997-35905P P 19970124  
JP 1998-511183 A3 19970822  
US 1997-922200 B2 19970902  
DK 1998-271 A 19980227  
US 1998-78422P P 19980318  
US 1998-82479P P 19980421  
US 1998-85789P P 19980518  
US 1999-258187 B1 19990225  
US 1999-258750 A2 19990226  
US 1999-265141 A2 19990308

OTHER SOURCE(S): MARPAT 135:273221

AB The present invention relates to human \*\*\*glucagon\*\*\* - \*\*\*like\*\*\* \*\*\*peptide\*\*\* -1 ( \*\*\*GLP\*\*\* - \*\*\*1\*\*\* ) derivs. having a \*\*\*lipophilic\*\*\* \*\*\*substituent\*\*\* , compns. contg. these derivs., and to methods for their prepn. A claimed compd. is His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Arg-Gly-Arg-Gly. Thus, coupling of \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37)-OH with Me(CH<sub>2</sub>)<sub>12</sub>CO-Glu(OSu)-OCMe<sub>3</sub> (Su = succinimidyl) (prepn. given), followed by deesterification with CF<sub>3</sub>CO<sub>2</sub>H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH<sub>2</sub>)<sub>12</sub>CO-.gamma.-Glu]26,34- \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37)-OH. Several prep'd. lipophilic \*\*\*GLP\*\*\* - \*\*\*1\*\*\* analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic \*\*\*GLP\*\*\* - \*\*\*1\*\*\* deriv. selected. The efficacy of several prep'd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human \*\*\*GLP\*\*\* - \*\*\*1\*\*\* receptor.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:566665 CAPLUS

DOCUMENT NUMBER: 135:122756

TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles

INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Kaarsholm, Niels C.; Olsen, Helle Birk; Bjorn, Soren Erik; Pedersen, Freddy

Zimmerdahl; Madsen, Kjeld

PATENT ASSIGNEE(S): Den.

SOURCE: U.S. Pat. Appl. Publ., 133 pp., Cont.-in-part of U.S.  
Ser. No. 265,141.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001011071	A1	20010802	US 1999-398111	19990916
US 6458924	B2	20021001		
WO 9808871	A1	19980305	WO 1997-DK340	19970822
			W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM	
			RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG	
JP 2001011095	A2	20010116	JP 2000-152778	19970822
US 6268343	B1	20010731	US 1999-258750	19990226
US 6384016	B1	20020507	US 1999-265141	19990308
US 2002025933	A1	20020228	US 2001-908534	20010718
PRIORITY APPLN. INFO.:		DK 1996-931	A 19960830	
		DK 1996-1259	A 19961108	
		DK 1996-1470	A 19961220	
		US 1997-36255P	P 19970124	
		US 1997-36226P	P 19970125	
		US 1998-84357P	P 19970822	
		WO 1997-DK340	W 19970822	
		US 1997-918810	B2 19970826	
		DK 1998-263	A 19980227	
		DK 1998-264	A 19980227	
		DK 1998-268	A 19980227	
		US 1998-38432	B2 19980311	
		US 1998-78422P	P 19980318	
		US 1998-82478P	P 19980421	
		US 1998-82479P	P 19980421	
		US 1998-82480P	P 19980421	
		US 1998-82802P	P 19980423	
		US 1999-258750	A2 19990226	
		US 1999-265141	A2 19990308	

US 1997-35905P P 19970124  
JP 1998-511183 A3 19970822  
US 1997-922200 B2 19970902  
DK 1998-271 A 19980227  
DK 1998-272 A 19980227  
DK 1998-274 A 19980227  
EP 1998-610006 A 19980313  
DK 1998-508 A 19980408  
DK 1998-509 A 19980408  
US 1998-85789P P 19980518  
US 1999-258187 B1 19990225

OTHER SOURCE(S): MARPAT 135:122756

AB The present invention relates to pharmaceutical compns. comprising lipophilic human \*\*\*glucagon\*\*\* - \*\*\*like\*\*\* \*\*\*peptide\*\*\* -1 ( \*\*\*GLP\*\*\* - \*\*\*1\*\*\* ) derivs. having a \*\*\*lipophilic\*\*\* \*\*\*substituent\*\*\* and a surfactant. Thus, coupling of \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37)-OH with Me(CH<sub>2</sub>)<sub>12</sub>CO-Glu(OSu)-OCMe<sub>3</sub> (Su = succinimidyl) (prepn. given), followed by deesterification with CF<sub>3</sub>CO<sub>2</sub>H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH<sub>2</sub>)<sub>12</sub>CO-<sub>gamma</sub>-Glu]26,34- \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37)-OH. Several prep'd. lipophilic \*\*\*GLP\*\*\* - \*\*\*1\*\*\* analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic \*\*\*GLP\*\*\* - \*\*\*1\*\*\* deriv. selected. The efficacy of several prep'd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human \*\*\*GLP\*\*\* - \*\*\*1\*\*\* receptor.

L11 ANSWER 4 OF 8 MEDLINE

DUPLICATE 2

ACCESSION NUMBER: 2000256912 MEDLINE

DOCUMENT NUMBER: 20256912 PubMed ID: 10794683

TITLE: Potent derivatives of glucagon-like peptide-1 with pharmacokinetic properties suitable for once daily administration.

AUTHOR: Knudsen L B; Nielsen P F; Huusfeldt P O; Johansen N L; Madsen K; Pedersen F Z; Thogersen H; Wilken M; Agerso H

CORPORATE SOURCE: Department of Molecular Pharmacology, Health Care Discovery

and Preclinical Development, Novo Nordisk A/S, Novo Park,  
DK-2760 Maaloev, Denmark.. lbkn@novo.dk

SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (2000 May 4) 43 (9) 1664-9.

Journal code: 9716531. ISSN: 0022-2623.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals  
ENTRY MONTH: 200006  
ENTRY DATE: Entered STN: 20000706  
Last Updated on STN: 20000706  
Entered Medline: 20000629

AB A series of very potent derivatives of the 30-amino acid peptide hormone \*\*\*glucagon\*\*\* - \*\*\*like\*\*\* \*\*\*peptide\*\*\* -1 ( \*\*\*GLP\*\*\* - \*\*\*1\*\*\* ) is described. The compounds were all derivatized with \*\*\*fatty\*\*\* \*\*\*acids\*\*\* in order to protract their action by facilitating binding to serum albumin. \*\*\*GLP\*\*\* - \*\*\*1\*\*\* had a potency (EC(50)) of 55 pM for the cloned human \*\*\*GLP\*\*\* - \*\*\*1\*\*\* receptor. Many of the compounds had similar or even higher potencies, despite quite large \*\*\*substituents\*\*\*. All compounds derivatized with \*\*\*fatty\*\*\* \*\*\*acids\*\*\* equal to or longer than 12 carbon atoms were very protracted compared to \*\*\*GLP\*\*\* - \*\*\*1\*\*\* and thus seem suitable for once daily administration to type 2 diabetic patients. A structure-activity relationship was obtained. \*\*\*GLP\*\*\* - \*\*\*1\*\*\* could be derivatized with linear \*\*\*fatty\*\*\* \*\*\*acids\*\*\* up to the length of 16 carbon atoms, sometimes longer, almost anywhere in the C-terminal part without considerable loss of potency. Derivatization with two \*\*\*fatty\*\*\* \*\*\*acid\*\*\* \*\*\*substituents\*\*\* led to a considerable loss of potency. A structure-activity relationship on derivatization of specific amino acids generally was obtained. It was found that the longer the \*\*\*fatty\*\*\* \*\*\*acid\*\*\*, the more potency was lost. Simultaneous modification of the N-terminus (in order to obtain better metabolic stability) interfered with \*\*\*fatty\*\*\* \*\*\*acid\*\*\* derivatization and led to loss of potency.

L11 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:566077 CAPLUS

DOCUMENT NUMBER: 131:194808

TITLE: GLP-1 derivatives of GLP-1 and exendin with a protracted profile of action

INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Madsen, Kjeld

PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943708	A1	19990902	WO 1999-DK86	19990225

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9932477 A1 19990915 AU 1999-32477 19990225

EP 1056775 A1 20001206 EP 1999-936077 19990225

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

ZA 9901571 A 19990902 ZA 1999-1571 19990226

US 2001047084 A1 20011129 US 2001-886311 20010621

PRIORITY APPLN. INFO.: DK 1998-274 A 19980227

US 1998-84357P P 19980505

WO 1999-DK86 W 19990225

US 1999-312177 B1 19990514

AB The present invention relates to derivs. exendin and of \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-C), wherein C is 35 or 36, which derivs. have just one \*\*\*lipophilic\*\*\* \*\*\*substituent\*\*\* which is attached to the C-terminal amino acid residue. The derivs. have a protracted action relative to \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37) and are useful for treating insulin-dependent and noninsulin-dependent diabetes mellitus. The derivs. of the invention can be combined with other antidiabetics or oral hypoglycemic agents. Pharmaceutical formulations contg. the derivs. of the invention are also claimed.

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:566075 CAPLUS

DOCUMENT NUMBER: 131:200093

TITLE: Preparation of GLP-1 analogs for treatment of obesity and non-insulin dependent diabetes mellitus

INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin; Pedersen, Freddy Zimmerdahl

PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.

SOURCE: PCT Int. Appl., 270 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9943706	A1	19990902	WO 1999-DK82	19990225
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9926106	A1	19990915	AU 1999-26106	19990225
EP 1060191	A1	20001220	EP 1999-906076	19990225
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, FI, RO				
ZA 9901569	A	19990827	ZA 1999-1569	19990226
ZA 9901570	A	19990902	ZA 1999-1570	19990226
PRIORITY APPLN. INFO.: DK 1998-268 A 19980227				
WO 1999-DK82 W 19990225				
OTHER SOURCE(S): MARPAT 131:200093				
AB ***GLP*** - ***1*** analog derivs. His-Xaa8-Xaa9-Gly-Xaa11-Phe-Thr-Xaa14-Asp-Xaa16-Xaa17-Xaa18-Xaa19-Xaa20-Xaa21-Xaa22-Xaa23-Xaa24-Xaa25-Xaa26-Xaa27-Phe-Ile-Xaa30-Xaa31-Xaa32-Xaa33-Xaa34-Xaa35-Xaa36-Xaa37-Xaa38-				
Xaa39-Xaa40-Xaa41-Xaa42-Xaa43-Xaa44-Xaa45 [Xaa represents an amino acid residue, e.g., Xaa8, Xaa25, Xaa30 = Ala, Gly, Ser, Thr, Leu, Ile, Val, Glu, Asp, Lys; Xaa9, Xaa21, Xaa27 = Glu, Asp, Lys; Xaa11 = Thr, Ala, Gly, Ser, Leu, Ile, Val, Glu, Asp, Lys; Xaa14, Xaa17, Xaa18 = Val, Ala, Gly, Ser, Thr, Leu, Ile, Tyr, Glu, Asp, Lys] having a ***lipophilic*** ***substituent*** were prep'd. for the treatment of obesity and non-insulin dependent diabetes mellitus. Thus, Arg26-34,Lys36[N.epsilon.-[.gamma.-glutamyl(N.alpha.-hexadecanoyl)]] ***GLP*** - ***1*** (7-36)-OH was prep'd. via reaction of Arg26-34,Lys36 ***GLP*** - ***1*** (7-36)-OH with Pal-Glu(ONSu)-But (Pal = hexadecanoyl, NSU = succinimide residue). The synthesized compds. have a protracted profile of action relative to ***GLP*** - ***1*** (7-37).				
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS				
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT				

L11 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1999:566074 CAPLUS  
 DOCUMENT NUMBER: 131:194807  
 TITLE: Insulinotropic N-terminally truncated GLP-1 lipophilic derivatives with protracted action  
 INVENTOR(S): Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf

PATENT ASSIGNEE(S): Novo Nordisk A/s, Den.

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9943705	A1	19990902	WO 1999-DK81	19990225
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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM  
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9926105	A1	19990915	AU 1999-26105	19990225
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EP 1056774	A1	20001206	EP 1999-906075	19990225
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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI

JP 2002508162	T2	20020319	JP 2000-533455	19990225
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PRIORITY APPLN. INFO.: DK 1998-264 A 19980227

DK 1998-509 A 19980408

WO 1999-DK81 W 19990225

OTHER SOURCE(S): MARPAT 131:194807

AB The present invention relates to N-terminally truncated derivs. of human \*\*\*glucagon\*\*\* - \*\*\*like\*\*\* \*\*\*peptide\*\*\* -1 ( \*\*\*GLP\*\*\* - \*\*\*1\*\*\* ) and analogs thereof having a protracted profile of action, as well as the use of such derivs. in pharmaceutical compns. for the treatment of obesity, insulin dependent or non-insulin dependent diabetes mellitus. The \*\*\*GLP\*\*\* - \*\*\*1\*\*\* derivs. have a \*\*\*lipophilic\*\*\* \*\*\*substituent\*\*\* attached to at least one amino acid residue.

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:163616 CAPLUS

DOCUMENT NUMBER: 128:244341

TITLE: Preparation of lipophilic human glucagon-like peptide-1 derivatives with protracted action profiles

INVENTOR(S): Knudsen, Liselotte Bjerre; Sorensen, Per Olaf; Nielsen, Per Franklin

PATENT ASSIGNEE(S): Novo Nordisk A/S, Den.; Knudsen, Liselotte Bjerre;

Sorensen, Per Olaf; Nielsen, Per Franklin

SOURCE: PCT Int. Appl., 76 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 11

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9808871	A1	19980305	WO 1997-DK340	19970822
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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,  
DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ,  
LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL,  
PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,  
UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR,  
GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA,  
GN, ML, MR, NE, SN, TD, TG

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R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,  
SI, LT, LV, FI, RO

CN 1232470	A	19991020	CN 1997-198413	19970822
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PRIORITY APPLN. INFO.: DK 1996-931 A 19960830

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AB Lipophilic human \*\*\*glucagon\*\*\* - \*\*\*like\*\*\* \*\*\*peptide\*\*\* -1 ( \*\*\*GLP\*\*\* - \*\*\*1\*\*\* ) derivs. and analogs thereof having a \*\*\*lipophilic\*\*\* \*\*\*substituent\*\*\* have interesting pharmacol. properties, in particular they have a more protracted profile of action than \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37). Thus, coupling of \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37)-OH with Me(CH<sub>2</sub>)<sub>12</sub>CO-Glu(OSu)-OCMe<sub>3</sub> (Su = succinimidyl) (prepn. given), followed by deesterification with CF<sub>3</sub>CO<sub>2</sub>H and chromatog. purifn. gave 8% bis-adduct Lys[Me(CH<sub>2</sub>)<sub>12</sub>CO-.gamma.-Glu]26,34- \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37)-OH (NNC 90-1167). Several prep'd. lipophilic \*\*\*GLP\*\*\* - \*\*\*1\*\*\* analogs were tested for protracted plasma concn. in pigs and were found to be much more persistent than \*\*\*GLP\*\*\* - \*\*\*1\*\*\* (7-37). In addn., the time of peak plasma concn. was found to vary within wide limits depending on the particular lipophilic \*\*\*GLP\*\*\* - \*\*\*1\*\*\* deriv. selected. The efficacy of several prep'd. derivs. was tested by stimulation of cAMP in a cell line expressing cloned human \*\*\*GLP\*\*\* - \*\*\*1\*\*\* receptor.

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(FILE 'HOME' ENTERED AT 17:44:50 ON 24 FEB 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA'  
ENTERED AT

17:45:13 ON 24 FEB 2003

L1 10431 S (GLUCAGON-LIKE PEPTIDE) OR GLP-1 OR GLP-2  
L2 1546 S LIPOPHILIC (W) (SUBSTITUENT OR GROUP)  
L3 704208 S FATTY ACID

L4 8 S L1 (P) L2  
L5 237276 S (SUCCINIC ACID) OR GLU OR ASP OR LYS OR GLY-LYS  
L6 881 S L5 (P) SPACER  
L7 5 S L1 (P) L3 (P) SUBSTITUENT  
L8 13 S L4 OR L7  
L9 0 S L8 (P) L6  
L10 0 S L8 (P) SPACER  
L11 8 DUPLICATE REMOVE L8 (5 DUPLICATES REMOVED)

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